

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

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Ex parte JIA-HE LI and JIE ZHANG

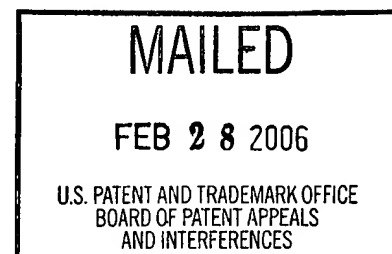
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Appeal No. 2005-1516  
Application No. 09/182,645

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ON BRIEF

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Before ELLIS, MILLS, and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 46-49 which are all of the claims on appeal<sup>1</sup> in this application.

These claims read as follows:

46. A method of treating neural or cardiac tissue damage resulting from a disease or condition in a mammal in need thereof, comprising administering to said mammal a therapeutically effective amount of an inhibitor of poly(ADP-ribose) glucosylase.
47. The method of claim 46, wherein the disease or condition is ischemia, reperfusion injury, neurodegenerative disease, neurological disease, head trauma, cardiovascular disease, heart attack, and vascular stroke.

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<sup>1</sup> Claims 1-25, 28-31 and 35-38 have been withdrawn from consideration by the examiner but are still pending. Claims 26-27, 32-34 and 39-45 are cancelled.

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48. The method of claim 47, wherein the disease or condition is ischemia.
49. The method of claim 47, wherein the disease or condition is reperfusion injury.

The prior art references cited by the examiner are:

Wang	1077644 CH	Oct. 27, 1993
Ning	1113711 CH	Dec. 27, 1995
Tanuma 1	3-205402 JP	Sept. 6, 1991
Tanuma 2	4-13684 JP	Jan. 17, 1992

Wen et al. (Wen), "Ginseng root prevents learning disability and neuronal loss in gerbils with 5 minute forebrain ischemia," Acta Neuropathol., Vol. 91, pp. 15-22 (1996).

Kim et al. (Kim), "Effects of Ginseng on Global Myocardial Ischemia and Reperfusion in the Rat Heart," J. Pharm Soc. Korea, Vol. 32, No. 1, pp. 70-79 (1988) [BIOSIS Abstract Only].

#### Grounds of Rejection

I. Claims 46-49 stand rejected under 35 U.S.C. §112, first paragraph for lack of enablement.

II. Claims 46-49 stand rejected under 35 U.S.C. §102(b) over Wang, Ning and Tanuma 1 and 2.

III. Claims 46-49 stand rejected under 35 U.S.C. §103(a) over Wang, Ning, Tanuma 1 and 2 in further view of Kim and Wen.

We reverse rejections I-III.

## DISCUSSION

### Background

Poly(ADP-ribose) glucohydrolase inhibitors are also known as PARG inhibitors. Specification, page 1. The DNA repair enzyme, poly (ADP-ribose) polymerase<sup>2</sup> or PARP “has emerged as a major player along the continuum of cell death. Cleavage of PARP by caspase-3 is a defining characteristic of apoptosis, and PARP also plays a pivotal role in classical necrotic cell death.” Specification, page 3. “Nuclear PARP is selectively activated by DNA strand breaks to catalyze the addition of long, branched chains of poly(ADP-ribose) from its substrate nicotinamide adenine dinucleotide (NAD) to a variety of nuclear proteins, most notably PARP itself. Massive DNA damage, such as that typically resulting from necrotic stimuli, elicits a major augmentation of PARP activity which rapidly depletes cellular levels of NAD. Depletion of NAD, an important co-enzyme in energy metabolism, results in lower ATP production. Furthermore, the cell consumes ATP in efforts to re-synthesize NAD, and this energy crisis culminates in cell death.” Specification, page 3.

“Upon binding to breaks in DNA, PARP activity is increased as much as 500 fold as it catalyzes the transfer and polymerization of ADP-ribose units onto both itself and other nuclear proteins.” Specification, pages 4-5. The activation of PARG “promotes

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<sup>2</sup> PARP is also known as poly (ADP-ribose) synthetase or poly (ADP-ribose) transferase.

the PARP-induced depletion of cellular energy, increased cell damage and cell death associated with disease and disorders linked to PARP activity.” Specification, page 6.

“The rapid activation of PARG in response to PAR synthesis and PARP activation indicates that PAR degradation via PARG should promote disorders and diseases associated with PARP activity. Accordingly, PARG inhibitors should be useful in down-regulating PARP by decreasing substrate and targets for PARP activity, and thus PARG inhibitors are useful for treating disorders and diseases associated with PARP activity...”. Specification, page 9.

According to the specification, “[i]t has been reported that PARP activation plays a key role in both NMDA- and NO-induced neurotoxicity.... The potential role of PARP inhibitors in treating neurodegenerative diseases and head trauma has thus been known.” Specification, pages 9-10. “PARG inhibitors should influence PARP-associated NMDA- and NO-induced neurotoxicity by downregulating PARP activity and thus PARG inhibitors are useful for treating neurodegenerative diseases, head trauma and cerebral ischemia.” Specification, page 10.

“Neural damage following stroke and other neurodegenerative processes are thought to result from a massive release of the excitatory neurotransmitter glutamate, which acts upon the N-methyl-D-aspartate (NMDA) receptors... Neurons release glutamate in great quantities when they are deprived of oxygen, as may occur during an ischemic brain insult such as a stroke or heart attack.” Specification, page 12. “The stimulation of NMDA receptors, in turn, activates the enzyme neuronal nitric oxide

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synthase (NNOS) which causes the formation of nitric oxide (NO) which more directly mediates neurotoxicity.” Specification, page 14.

### Procedural History

On Dec. 1, 1999, a restriction and election of species requirement was mailed to appellants. Appellants elected prosecution of the composition claims and chose lignin glycoside as the species of PARG inhibitor. Paper No. 9, February 2, 2000. A Final rejection issued in the application on November 30, 2001, and an Appeal Brief was filed in response to the Final rejection on May 10, 2002. A new Non-final rejection reopening prosecution was issued by the examiner on August 7, 2002. Appellants requested that the original appeal be reinstated. The examiner issued an Answer on April 21, 2003. A Reply Brief was filed by Appellants on October 10, 2003, responding to new issues raised in the new Non-final rejection of August 7, 2002.

### Enablement

I. Claims 46-49 stand rejected under 35 U.S.C. §112, first paragraph for lack of enablement of the claims throughout their entire scope. The examiner argues that the specification does not reasonably provide enablement for PARG inhibitors, in general. Paper No. 29, Non-final Rejection, page 2.

We note, however, that given the election of species, we need only consider the claims to the extent that they are directed to lignin glycoside. Thus, the examiner’s

rejection of the claims for lack of enablement for other PARG inhibitors is not ripe for consideration. Accordingly, we take no position with respect to whether the specification would have enabled one skilled in the art to "make and use" PARG inhibitors in general. See Ex parte Ohsaka, 2 USPQ2d 1460, 1461 (Bd. Pat. App. & Int. 1987).

In view of the foregoing, we reverse the rejection for lack of enablement

#### Anticipation

Claims 46-49 stand rejected under 35 U.S.C. §102(b) over Wang or Ning.

According to the examiner,

Wang teaches [a] method of treating diabetes comprising administering ginseng in the form of tea to the patient. ... A tea bag containing 1.8 gram of ginseng [g] powders and extract. See page 3, the application example of the English Translation. Ning teaches [a] method of treatment of ischemia comprising administering ginseng in the form of tea to a patient. See the abstract. A tea bag weigh[ing] about 15 g, which contains about 1% of ginseng extract. See, page 2, the last paragraph bridging to page 3, the third paragraph of the English translation. The ginseng is administered in the form of tea. See both abstracts. Tanuma teach that ginseng hot water extract contain[s] the lignin glycoside herein. ... Therefore, the claimed method herein read[s] on the method of Wang and Ning.

Non-final, page 4. Appearing to rely on principles of inherency, though not specifically stated, we understand the examiner to argue that Tanuma 1 and 2 teach that the ginseng hot water extract contains lignin glycoside. Thus the examiner appears to argue that the teas of Wang and Ning (ginseng water extracts) provide lignin glycoside to the patient.

In our view the examiner has not met his burden of proof to establish a prima facie case of anticipation or provided any evidence that a water extract of ginseng contains a therapeutically effective amount of lignin glycoside. The process of obtaining lignin glycoside as set forth both in the specification and in Tanuma 1 and 2 is a multistep process. As pointed out by appellants, lignin glycoside is not present in a hot water extract of a crude vegetative product (such as a pine cone, ginseng, etc.). Reply Brief, page 4. Appellants argue that, Tanuma 1 discloses that the vegetative "material is treated in the solvent (for example, hot water, ethanol, acetone). The treating time is about 1 to 15 hours. The treated material is extracted in an alkaline solution (0.1 to 1N sodium hydroxide, ammonium, etc.)." Tanuma 1, page 5, lines 5-12. We find no indication that the teas of Wang or Ning are steeped for 1-15 hours and, certainly, no teaching that the tea was extracted with an alkaline solution.

In addition, with respect to the teachings of Wang, we do not find that the examiner has provided any evidence that the diabetes patients described therein are patients having neural or cardiac tissue damage (claim 46), or that said patients suffer from any of the conditions recited in claims 47-49. Thus, Wang does not reasonably appear to describe each element of the claimed method.

While Ning, unlike Wang, treats patients suffering from ischemia (claim 47), however, as discussed above we do not find that the examiner has established a prima facie case of anticipation based on Ning under the principles of inherency based on Tanuma 1 and 2. In addition, we point out that the coffee-tasting tea of Ning includes

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multiple ingredients. That is, addition to ginseng, the tea of Ning further comprises Acanthopanax root, or Acanthopanax Bark, or Acanthopanax extract, pilose antler blood or pilose antler extract, wolfberry fruit, sugar and citric acid. Ning, claim 1. Thus, it is not clear that lignin glycoside from the ginseng tea of Ning is present in an effective amount.

Thus, the examiner has not properly established a prima facie case of anticipation based on the principles of inherency. We remind the examiner that an inherent limitation is one that is necessarily present; inherency is not established by "probabilities or possibilities." Scaltech, Inc. v. Retec/Tetra, LLC., 178 F.3d 1378, 1384, 51 USPQ2d 1055, 1059 (Fed. Cir. 1999). As set forth in Continental Can Co. USA, Inc. v. Monsanto Co., 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749-50 (Fed. Cir. 1991) "The mere fact that a certain thing may result from a given set of circumstances is not sufficient." Instead, the natural result flowing from the method of preparing the tea of Wang or the coffee-tasting tea of Ning must result in a composition comprising an effective amount of the claimed lignin glycoside. We do not find the evidence of record supports that natural result on its face.

Therefore, the rejection of the claims for anticipation over Wang, Ning and Tanuma 1 and 2 is reversed.



Obviousness

Claims 46-49 stand rejected under 35 U.S.C. §103(a) over Wang, Ning, Tanuma 1 and 2 in further view of Kim and Wen.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness is established when the teachings from the prior art would have suggested the claimed subject matter to a person of ordinary skill in the art. In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). An obviousness analysis requires that the prior art both suggest the claimed subject matter and provide a reasonable expectation of success to one reasonably skilled in the art. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). With this as background, we analyze the prior art applied by the examiner in the rejection of the claims on appeal.

Wang, Ning and Tanuma 1 and 2 are discussed above. The examiner essentially puts forth the same arguments with respect to the obviousness rejection of the claims as were set forth concerning the anticipation of the claims by these references. We find the deficiencies noted with respect to the references in the anticipation context exist when the references are viewed with respect to the obviousness rejection. These noted deficiencies in Wang, Ning and Tanuma 1 and 2 are not overcome by their further combination with Wen and Kim. In our view the examiner has not provided a clear reason, suggestion or motivation to combine

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Tanuma 1 and 2, disclosing a purified lignin glycoside for the treatment of cancer with Wang, describing a tea for the treatment of diabetes, or Ning, a tea for the treatment of ischemia.

The examiner argues both Kim and Wen teach that a ginseng extract is useful for treating ischemia and/or reperfusion injury. Paper No. 29, Non-final, page 7. Wen describes the effects of red ginseng powder (RGP), crude ginseng saponin (CGS), crude ginseng non-saponin (CGNS), ginsenoside (Rb<sub>1</sub>) ginsenoside Rg<sub>1</sub> and ginsenoside Ro on response latency of neurons in ischemic gerbils. Page 17. The examiner has not indicated or shown that any of the ginsenosides or crude ginseng products of Wen contain lignin glycoside. The examiner has not pointed out any teaching or suggestion in the art to use the lignin glycoside taught by Tanuma 1 and 2 in Wen's patients. Nor has the examiner indicated how Wen makes up for any of the deficiencies noted in the combination of Wang, Ning and Tanuma 1 and 2.

We do not find on the record before us the examiner has made out a prima facie case of obviousness in view of Kim for reasons similar to those cited for Wen. In view of the above, the rejection of the claims over Wang, Ning, Tanuma 1 and 2 in further view of Kim and Wen is reversed.

#### Another Issue

On the record before us we do not find that the examiner has set forth sufficient facts to establish a prima facie case of obviousness in view of Kim. Upon return of the

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application, we recommend that the examiner review the disclosure of Kim to determine if it supports a prima facie case of anticipation based upon the principles of inherency in view of Tanuma 1.

In particular, unlike Wang, Ning and Wen, Kim describes an ethanol extract of ginseng for the treatment of ischemic hearts. Tanuma 1, page 4, shows a method involving an ethanol extraction of ginseng which results in the production of lignin glycoside. Upon return of the application it is recommended that the Examiner carefully review the full disclosure of Kim, and determine whether a prima facie case of anticipation or obviousness should be made in view of the teachings of Tanuma 1 and 2.

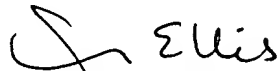
#### CONCLUSION

Therefore, the rejection for lack of enablement is reversed. Rejections I-III above of claims 46-49 are reversed. The application is returned to the examiner for further consideration of the patentability of the claims over Kim as evidenced by the teachings of Tanuma 1 and 2.

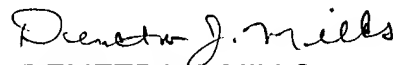
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No time period for taking any subsequent action in connection with this appeal  
may be extended under 37 CFR § 1.136(a).

REVERSED



JOAN ELLIS  
Administrative Patent Judge



DEMETRA J. MILLS  
Administrative Patent Judge



ERIC GRIMES  
Administrative Patent Judge

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